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EXAMINER	
STRZELECKA, TERESA E	
ART UNIT	**PAPER NUMBER**
1637	

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13

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/866,283	RUNDELL ET AL.	
	Examiner	Art Unit	
	Teresa E Strzelecka	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3-10,12-24 and 26-32* is/are pending in the application.

4a) Of the above claim(s) *12-22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10,23,24 and 26-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. This office action is in response to an amendment filed on May 30, 2003. Claims 1-32 were pending, with claims 12-22 withdrawn from consideration. Applicants cancelled claims 2, 11 and 25 and amended claims 1 and 24. Claims 1, 3-10, 12-24 and 26-32 are pending, with claims 12-22 withdrawn from consideration. Claims 1, 3-10, 23, 24 and 26-32 will be examined.

2. Applicants' amendments, claim cancellations and arguments overcame the following rejections: rejection of claims 1-11 and 23-32 under 35 U.S.C. 112, first paragraph; rejection of claims 1-11 and 23-32 under 35 U.S.C. 112, second paragraph. The following rejections are maintained: rejection of claims 1, 8-10 under 35 U.S.C. 102(b) over Hayatsu et al; rejection of claims 1, 8-10 under 35 U.S.C. 102(b) over Kariko et al.

3. The drawings were received on May 30, 2003. These drawings are accepted.

4. The objection to specification is withdrawn in view of Applicants' amendment.

5. This office action is made non-final because of new grounds for rejection. Applicants' arguments are addressed below, since they are pertinent to the new rejections.

Response to Arguments

6. Applicant's arguments regarding art rejections filed May 30, 2003 have been fully considered but they are not persuasive. In particular, Applicants argue that none of the references used for 102(b) and 103(a) rejections (Hayashida et al., van Gemen et al., Hayatsu et al; Kariko et al.) anticipate the limitations of "nucleic acid reference standard" and "target nucleic acid is not substantially detected in a nucleic acid assay". This argument is not considered persuasive.

The limitation of "reference standard" amounts to an intended use of the nucleic acid, and therefore is not considered when the invention is compared with prior art. A recitation of the intended use of the claimed invention must result in a structural difference between the claimed

invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim. In a claim drawn to a process of making, the intended use must result in a manipulative difference as compared to the prior art. See In re Casey, 152 USPQ 235 (CCPA 1967) and In re Otto, 136 USPQ 458, 459 (CCPA 1963). On the other hand, any nucleic acid can be used as a reference standard, therefore this is also an inherent characteristic of any nucleic acid.

Regarding the limitation "target nucleic acid is not substantially detected in a nucleic acid assay", any nucleic acid bound to a solid support and participating in a hybridization assay will be detected at a lower level from any nucleic acid in solution because of faster hybridization in solution, as evidenced by Matthews et al. on page 17, second paragraph (Anal. Biochem., vol. 169, pp. 1-25, 1988). Therefore, any nucleic acid bound to a solid support will inherently meet the limitation of not being substantially detected in a nucleic acid assay according to Applicants' definition.

Claim Objections

7. Claims 26-29 are objected to because of the following informalities: they depend from cancelled claim 25. Appropriate correction is required.

Claim interpretation

8. According to the explanation given above, claim 1 is being interpreted as drawn to an isolated target nucleic acid bound to a microparticulate binding agent, where the microparticulate binding agent is interpreted as meaning any solid support, since any solid material consists of microparticles.

Regarding a limitation of "an instructional material for the use thereof" in claims 23, 24 and 26-32, this is considered a printed matter which is not functionally related to the components of the

kit. A kit which simply contained the reference nucleic acids would have the completely identical functionality of the kit which had the instructions and contained the reference nucleic acids (see MPEP 2106. VI):

Nonfunctional descriptive material cannot render nonobvious an invention that would have otherwise been obvious. Cf. In re Gulack, 703 F.2d 1381, 1385, 217 USPQ 401, 404 (Fed. Cir. 1983) (when descriptive material is not functionally related to the substrate, the descriptive material will not distinguish the invention from the prior art in terms of patentability).

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 1 and 8-10 are rejected under 35 U.S.C. 102(b) as being anticipated by Hayatsu et al. (Chem. Pharm. Bull., vol. 45, p. 1363-68, 1997; cited in the previous office action).

Regarding claims 1 and 8, Hayatsu et al. teach genomic DNA (calf thymus and salmon testis) bound to chitosan. The nucleic acid-chitosan complex was insoluble and the nucleic acid was tightly bound to the chitosan (Abstract, page 1363).

Regarding claim 9, Hayatsu et al. teach linear DNA (page 1363, second paragraph).

Regarding claim 10, Hayatsu et al. teach that the complexes were used in a digestion assay with DNAse I and phosphodiesterase (page 1363, the last paragraph).

11. Claims 1 and 8-10 are rejected under 35 U.S.C. 102(b) as being anticipated by Kariko et al. (Biochim. Biophys. Acta, vol. 1369, p. 320-334, 1998; cited in the previous office action).

Regarding claims 1 and 8, Kariko et al. teach plasmid DNA or its mRNA transcript bound to cationic liposomes, composed of 1:1 mixture of DOTMA (N-[1-(2,3-dioleyloxy)propyl]-n,n,n-trimethyl-ammonium cloride) and DOPE (dioleoyl phosphatidylethanolamine) (Abstract, page 321, the last paragraph; page 322, paragraphs 1-3).

Regarding claim 9, Kariko et al. teach non-linear nucleic acid (DNA plasmid) and linear nucleic acid (mRNA) (page 321, the last paragraph).

Regarding claim 10, Kariko et al. teach that the complexes were used to treat HSO (human osteosarcoma cell line) cells to determine the effectiveness of transfection (page 322; Fig. 1).

12. Claims 1, 3, 5 and 7-10 are rejected under 35 U.S.C. 102(b) as being anticipated by Boom et al. (EP 0 819 696 A2).

Regarding claim 1, Boom et al. teach an isolated nucleic acid bound to silicon dioxide particles (= siliceous compound) (page 3, lines 41-50).

Regarding claims 1 and 3, Boom et al. teach isolated nucleic acid bound to a nylon filter (page 5, line 21; page 17, lines 36-56).

Regarding claim 5, Boom et al. teach isolated nucleic acid bound to diatomaceous earth (page 14, lines 50-56; page 15, lines 1-36).

Regarding claim 7, Boom et al. teach washing the nucleic acid bound to particles with 70% ethanol (page 3, lines 50-53).

Regarding claim 8, Boom et al. teach ribonucleic acid (page 2, lines 55-57; page 13, lines 14-24).

Regarding claim 9, Boom et al. teach linear and non-linear nucleic acids (page 9, lines 40-50).

Regarding claim 10, Boom et al. teach using the nucleic acid in a PCR assay (page 12, lines 50-56; page 16, lines 20-38; page 17, lines 36-54).

Claim Rejections - 35 USC § 103

13. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

14. Claim 4 is rejected under 35 U.S.C. 103(a) as being unpatentable over Boom et al. (EP 0 819 696 A2) and Holmberg (EP 0 514513 B1).

A) Regarding claim 4, Boom et al. teach isolated nucleic acid bound to polystyrene particles (page 5, lines 6-10; page 16, lines 20-38), but do not teach amine modified polystyrene.

B) Holmberg teaches binding of oligonucleotides to polystyrene solid support derivatized with an amino group (page 4, lines 25-31 and 44-53).

It would have been prima facie obvious to one of ordinary skill in the art at the time of the invention to have used amine modified polystyrene of Holmberg to bind nucleic acids of Boom et al. The motivation to do so, provided by Holmberg, would have been that amino group enabled covalent binding of silylated nucleoside to the solid support, which in turn enabled convenient synthesis and purification of full-length oligonucleotides (page 4, lines 32-36).

15. Claim 6 is rejected under 35 U.S.C. 103(a) as being unpatentable over Boom et al. (EP 0 819 696 A2) and Matsui et al. (Chemistry, Eur. J., vol. 7, pp. 1555-1560, April 2001).

A) Boom et al. do not teach low alumina zeolyte.

B) Matsui et al. teach adsorption (binding) of nucleic acids to low alumina zeolites (Table 1).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have used low alumina zeolites of Matsui et al. for binding of nucleic acids of Boom et al. The motivation to do so, provided by Matsui et al., would have been that zeolities selectively adsorbed nucleic acids, the adsorption was in the absence of high salt concentration and independent on pH (page 1559, second and third paragraph).

16. Claims 23, 24, 26, 28, and 30-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Boom et al. (EP 0 819 696 A2) and Stratagene Catalog (p. 39, 1988; cited in the previous office action).

A) Regarding claims 23 and 24, Boom et al. teach an isolated nucleic acid bound to silicon dioxide particles (= siliceous compound) (page 3, lines 41-50). Boom et al. teach a kit (= a combination of means) comprising for isolating nucleic acids (= producing a nucleic acid reference standard), the kit comprising a suspension of silica particles and reagents, such as ethanol (page 4, lines 20-35). Boom et al. teach making of the nucleic acid bound to microparticulate matter by addition of nucleic-acid containing sample to suspension of silica particles in a reaction vessel and separation of nucleic acid-particle complexes (page 3, lines 41-50). For example, 50 μL of DNA-containing sample were added to a test tube containing latex, silica or diatomaceous earth particles (page 6, lines 19-21 and 35-48). Boom et al. do not specifically teach an applicator, but since they teach addition of a certain volume of liquid to a test tube, which is accomplished with a pipettor, for example, in this case they used an applicator, therefore they teach production of a nucleic acid-microparticulate complex using an applicator.

Regarding claims 24 and 26, Boom et al. teach isolated nucleic acid bound to a nylon filter (page 5, line 21; page 17, lines 36-56).

Regarding claim 28, Boom et al. teach isolated nucleic acid bound to diatomaceous earth (page 14, lines 50-56; page 15, lines 1-36).

Regarding claim 30, Boom et al. teach washing the nucleic acid bound to particles with 70% ethanol (page 3, lines 50-53).

Regarding claim 31, Boom et al. teach ribonucleic acid (page 2, lines 55-57; page 13, lines 14-24).

Regarding claim 32, Boom et al. teach linear and non-linear nucleic acids (page 9, lines 40-50).

B) Boom et al. do not teach a kit comprising an isolated target nucleic acid.

C) Stratagene catalog teaches a motivation to combine reagents into kit format (page 39).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine the method of Boom et al. into a kit format as discussed by Stratagene catalog since the Stratagene catalog teaches a motivation for combining reagents of use in an assay into a kit, "Each kit provides two services: 1) a variety of different reagents have been assembled and pre-mixed specifically for a defined set of experiments. Thus one need not purchase gram quantities of 10 different reagents, each of which is needed in only microgram amounts, when beginning a series of experiments. When one considers all of the unused chemicals that typically accumulate in weighing rooms, desiccators, and freezers, one quickly realizes that it is actually far more expensive for a small number of users to prepare most buffer solutions from the basic reagents. Stratagene provides only the quantities you will actually need, premixed and tested. In actuality, the kit format saves money and resources for everyone by dramatically reducing waste. 2) The other service provided in a kit is quality control" (page 39, column 1).

17. Claim 27 is rejected under 35 U.S.C. 103(a) as being unpatentable over Boom et al. (EP 0 819 696 A2) in view of Stratagene Catalog (p. 39, 1988; cited in the previous office action) and Holmberg (EP 0 514513 B1).

A) Regarding claim 27, Boom et al. teach isolated nucleic acid bound to polystyrene particles (page 5, lines 6-10; page 16, lines 20-38), but do not teach amine modified polystyrene.

B) Holmberg teaches binding of oligonucleotides to polystyrene solid support derivatized with an amino group (page 4, lines 25-31 and 44-53).

It would have been prima facie obvious to one of ordinary skill in the art at the time of the invention to have used amine modified polystyrene of Holmberg to bind nucleic acids in a kit of Boom et al. The motivation to do so, provided by Holmberg, would have been that amino group enabled covalent binding of silylated nucleoside to the solid support, which in turn enabled convenient synthesis and purification of full-length oligonucleotides (page 4, lines 32-36).

18. Claim 29 is rejected under 35 U.S.C. 103(a) as being unpatentable over Boom et al. (EP 0 819 696 A2) in view of Stratagene Catalog (p. 39, 1988; cited in the previous office action) and Matsui et al. (Chemistry, Eur. J., vol. 7, pp. 1555-1560, April 2001).

A) Boom et al. do not teach low alumina zeolyte.

B) Matsui et al. teach adsorption (binding) of nucleic acids to low alumina zeolites (Table 1).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to have used low alumina zeolites of Matsui et al. for binding of nucleic acids of Boom et al. The motivation to do so, provided by Matsui et al., would have been that zeolities selectively adsorbed nucleic acids, the adsorption was in the absence of high salt concentration and independent on pH (page 1559, second and third paragraph).

19. Claims 23, 24, 31 and 32 are rejected under 35 U.S.C. 102(b) as being anticipated by Hayatsu et al. (Chem. Pharm. Bull., vol. 45, p. 1363-68, 1997; cited in the previous office action) in view of Stratagene Catalog (p. 39, 1988; cited in the previous office action).

A) Regarding claims 23 and 24, Hayatsu et al. teach genomic DNA (calf thymus and salmon testis) bound to chitosan. The nucleic acid-chitosan complex was insoluble and the nucleic acid was tightly bound to the chitosan (Abstract, page 1363). Hayatsu et al. teach preparation of nucleic acid-chitosan complexes by addition of drops of chitosan to DNA solution (page 1363, third paragraph). Hayatsu et al. do not specifically teach an applicator, but since they teach addition of a certain volume of chitosan solution to a vessel containing DNA solution, which is accomplished with a pipettor, for example, in this case they used an applicator, therefore they teach production of a nucleic acid-microparticulate complex using an applicator.

Regarding claim 31, Hayatsu et al. teach DNA (deoxyribonucleic acid).

Regarding claim 32, Hayatsu et al. teach linear DNA (page 1363, second paragraph).

B) Hayatsu et al. do not teach a kit comprising an isolated target nucleic acid.

C) Stratagene catalog teaches a motivation to combine reagents into kit format (page 39). It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine the method of Hayatsu et al. into a kit format as discussed by Stratagene catalog since the Stratagene catalog teaches a motivation for combining reagents of use in an assay into a kit, "Each kit provides two services: 1) a variety of different reagents have been assembled and pre-mixed specifically for a defined set of experiments. Thus one need not purchase gram quantities of 10 different reagents, each of which is needed in only microgram amounts, when beginning a series of experiments. When one considers all of the unused chemicals that typically accumulate in weighing rooms, desiccators, and freezers, one quickly realizes that it is actually far

more expensive for a small number of users to prepare most buffer solutions from the basic reagents. Stratagene provides only the quantities you will actually need, premixed and tested. In actuality, the kit format saves money and resources for everyone by dramatically reducing waste. 2) The other service provided in a kit is quality control" (page 39, column 1).

20. Claims 23, 24, 31 and 32 are rejected under 35 U.S.C. 102(b) as being anticipated by Kariko et al. (Biochim. Biophys. Acta, vol. 1369, p. 320-334, 1998; cited in the previous office action) in view of Stratagene Catalog (p. 39, 1988; cited in the previous office action).

Regarding claims 23 and 24, Kariko et al. teach plasmid DNA or its mRNA transcript bound to cationic liposomes, composed of 1:1 mixture of DOTMA (N-[1-(2,3-dioleyloxy)propyl]-n,n,n-trimethyl-ammonium cloride) and DOPE (dioleoyl phosphatidylethanolamine), lipofectin (Abstract, page 321, the last paragraph; page 322, paragraphs 1-3). Kariko et al. teach making of the lipofectin-nucleic acid complex by addition of 0.23 μg of nucleic acid from 0.07 μg/ μl solution to lipofectin (page 322, third paragraph). Kariko et al. do not specifically teach an applicator, but since they teach addition of a certain volume of nucleic acid solution to a vessel containing lipofectin, which is accomplished with a pipettor, for example, in this case they used an applicator, therefore they teach production of a nucleic acid-microparticulate complex using an applicator.

Regarding claim 31, Kariko et al. teach DNA (deoxyribonucleic acid) and mRNA (ribonucleic acid) (page 321, the last paragraph).

Regarding claim 32, Kariko et al. teach non-linear nucleic acid (DNA plasmid) and linear nucleic acid (mRNA) (page 321, the last paragraph).

B) Kariko et al. do not teach a kit comprising an isolated target nucleic acid.

C) Stratagene catalog teaches a motivation to combine reagents into kit format (page 39).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine the method of Kariko et al. into a kit format as discussed by Stratagene catalog since the Stratagene catalog teaches a motivation for combining reagents of use in an assay into a kit, "Each kit provides two services: 1) a variety of different reagents have been assembled and pre-mixed specifically for a defined set of experiments. Thus one need not purchase gram quantities of 10 different reagents, each of which is needed in only microgram amounts, when beginning a series of experiments. When one considers all of the unused chemicals that typically accumulate in weighing rooms, desiccators, and freezers, one quickly realizes that it is actually far more expensive for a small number of users to prepare most buffer solutions from the basic reagents. Stratagene provides only the quantities you will actually need, premixed and tested. In actuality, the kit format saves money and resources for everyone by dramatically reducing waste. 2) The other service provided in a kit is quality control" (page 39, column 1).

21. No claims are allowed.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Teresa E Strzelecka whose telephone number is (703) 306-5877. The examiner can normally be reached on M-F (8:30-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (703) 308-1119. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

TS
September 14, 2003

TS

JEFFREY FREDMAN
PRIMARY EXAMINER